

BIOLOGY OF THE BASEMENT MEMBRANE ZONE OF SKIN AND  
EPIDERMOLYSIS BULLOSA  
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National Institute of Arthritis and Musculoskeletal and Skin Diseases National  
Institute of Child Health and Human Development

## I. PURPOSE

The Skin Diseases Program of the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) supports research on the structure, function, and diseases of the skin. The Genetics and Teratology Branch of the National Institute of Child Health and Human Development (NICHD) supports research on genetic and congenital malformations of skin. This program announcement is to encourage submission of research grant applications in the area of basement membrane zone of the skin in normal and diseased states with particular reference to epidermolysis bullosa.

## II. BACKGROUND

The basement membrane zone of the skin is an area of great biologic importance. The many structures within this zone mediate not only attachment of the epidermis to the underlying dermis but also transport nutrients from the vasculature of the dermis to the nonvascularized epidermis and, in the reverse direction, chemicals, including drugs, into the systemic circulation following topical application. Studies of skin diseases must consider the basement membrane zone in evaluating the underlying mechanisms of their pathogenesis.

Epidermolysis bullosa is a large group of hereditary and at least two acquired skin diseases in which the pathologic defect occurs within the skin basement membrane zone, either within the basal keratinocytes, the electron microscopically identified basement membrane, or the superficial papillary dermis. In the past several years many structures have been identified within this area of skin. Several have been implicated in the pathogenesis of one or more forms of epidermolysis bullosa. Thus, these diseases represent an experiment of nature, the study of which can provide great insights into normal functioning of molecules of the basement membrane zone of skin, as well as potential approaches to the diagnosis and treatment of individuals suffering with these often debilitating or even fatal conditions.

The NIAMS supports a National Epidermolysis Bullosa Registry that consists of four clinical sites and a coordinating center. The first five years of this Registry

will conclude in September 1991. The Registry facilitates research in epidermolysis bullosa and the biology of the basement membrane zone by providing tissues from banked sources and/or obtaining patients interested in participating in research.

## RESEARCH GOALS AND SCOPE

The goal of this program announcement is to stimulate research in the biology of the skin basement membrane zone and into the etiopathogenesis of epidermolysis bullosa. Some research areas appropriate for inclusion in applications responsive to this announcement are:

- o Studies of the molecules making up the basement membrane zone, in the normal and/or diseased state;
- o Studies seeking early aberrations and biological markers of skin development at the tissue, cellular, and molecular levels;
- o Molecular genetic approaches to understanding basic defects in the hereditary forms of epidermolysis bullosa utilizing both candidate gene and anonymous marker approaches;
- o Investigations utilizing tissue culture, organ and animal model systems, and other techniques as appropriate to investigate the mechanisms by which defects in the skin basement membrane zone result in disease phenotype;
- o Studies leading to clinical trials and the treatment of various forms of epidermolysis bullosa;
- o Epidemiology of subsets of epidermolysis bullosa.

## MECHANISM OF SUPPORT

Research mechanisms to support these investigations include individual research grants (RO1), Clinical Investigator Awards (KO8), and First Independent Research and Transition (FIRST) Awards (R29).

## SPECIAL INSTRUCTIONS TO APPLICANTS REGARDING IMPLEMENTATION OF NIH POLICIES CONCERNING INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH STUDY POPULATIONS

NIH and ADAMHA policy is that applicants for NIH/ADAMHA clinical research grants and cooperative agreements will be required to include minorities and women in study populations so that research findings can be of benefit to all

persons at risk of the disease, disorder or condition under study; special emphasis should be placed on the need for inclusion of minorities and women in studies of diseases, disorders and conditions which disproportionately affect them. This policy is intended to apply to males and females of all ages. If women or minorities are excluded or inadequately represented in clinical research, particularly in proposed population-based studies, a clear compelling rationale should be provided.

The composition of the proposed study population must be described in terms of gender and racial/ethnic group. In addition, gender and racial/ethnic issues should be addressed in developing a research design and sample size appropriate for the scientific objectives of the study. This information should be included in the form PHS 398 in Section 2, A-D of the Research Plan AND summarized in Section 2, E, Human Subjects. Applicants/offerors are urged to assess carefully the feasibility of including the broadest possible representation of minority groups. However, NIH recognizes that it may not be feasible or appropriate in all research projects to include representation of the full array of United States racial/ethnic minority populations (i.e., Native Americans (including American Indians or Alaskan Natives), Asian/Pacific Islanders, Blacks, Hispanics).

The rationale for studies on single minority population groups should be provided.

For the purpose of this policy, clinical research includes human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials.

The usual NIH policies concerning research on human subjects also apply. Basic research or clinical studies in which human tissues cannot be identified or linked to individuals are excluded. However, every effort should be made to include human tissues from women and racial/ethnic minorities when it is important to apply the results of the study broadly, and this should be addressed by applicants.

For foreign awards, the policy on inclusion of women applies fully; since the definition of minority differs in other countries, the applicant must discuss the relevance of research involving foreign population groups to the United States' populations, including minorities.

If the required information is not contained within the application, the application will be returned.

Peer reviewers will address specifically whether the research plan in the application conforms to these policies. If the representation of women or minorities in a study design is inadequate to answer the scientific question(s) addressed AND the justification for the selected study population is inadequate, it will be considered a scientific weakness or deficiency in the study design and will be reflected in assigning the priority score to the application.

All applications for clinical research submitted to NIH are required to address these policies. NIH funding components will not award grants or cooperative agreements that do not comply with these policies.

## APPLICATION AND REVIEW PROCEDURES

Applications in response to this announcement will be reviewed in accordance with Public Health Service peer review procedures for research grants. Review criteria include significance and originality of the research goals and approaches; feasibility of the research and adequacy of the experimental design; training, research competence, and dedication of the investigator(s); adequacy of available facilities; and provision for the humane care of animals. Decisions will be based on initial review group and National Advisory Council recommendations. Applications must be submitted on form PHS 398 (rev. 10/88), available in the business or grants office at most academic or research institutions and from the Division of Research Grants, National Institutes of Health, Westwood Building, Room 449, Bethesda, MD 20894, telephone (301) 496-7441.

Applications will be accepted in accordance with the submission dates for new applications on a continuing basis.

February 1, June 1, October 1 for research grant applications.

The phrase "BIOLOGY OF THE BASEMENT MEMBRANE ZONE OF SKIN AND EPIDERMOLYSIS BULLOSA, PA-91-67" must be typed on line 2 of the face page of the application. The original and six copies must be sent or delivered to:

Grant Application Receipt Office  
Division of Research Grants  
Westwood Building, Room 240  
National Institutes of Health  
Bethesda, MD 20892-4500\*\*

For further information, investigators are encouraged to contact the following individuals:

Alan N. Moshell, M.D.  
Skin Diseases Program Director  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 405  
Bethesda, MD 20892  
Telephone: (301) 496-7326

Delbert H. Dayton, M.D.  
Genetics and Teratology Branch  
Center for Research for Mothers and Children  
National Institute of Child Health and Human Development  
Executive Plaza North Building, Room 643  
9000 Rockville Pike  
Bethesda, MD 20892  
Telephone: (301) 496-5541

For fiscal and administrative matters, contact:

Diane M. Watson  
Grants Management Officer  
National Institute of Arthritis and Musculoskeletal and Skin Diseases  
Westwood Building, Room 407-A  
Bethesda, MD 20892  
Telephone: (301) 496-7495

Douglas Shawver  
Supervisory Grants Management Specialist  
Grants Management Branch  
Office of Grants and Contracts  
National Institute of Child Health and Human Development  
Executive Plaza North, Room 505  
Bethesda, MD 20892  
Telephone: (301) 496-1303

This program is described in the Catalog of Federal Domestic Assistance No.93.846, Arthritis, Musculoskeletal and Skin Diseases Research and No. 93.865, Research for Mothers and Children. Awards will be made under authorization of the Public Health Service Act, Title III, Section 301(c) (Public Law 78-410, as amended; 42 USC 241) and administered under PHS grants policies and Federal Regulations 42 CFR Part 52 and 45 CFR Part 74. This program is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review.

**\*\*THE MAILING ADDRESS GIVEN FOR SENDING APPLICATIONS TO THE  
DIVISION OF RESEARCH GRANTS OR CONTACTING PROGRAM STAFF IN**

THE WESTWOOD BUILDING IS THE CENTRAL MAILING ADDRESS FOR THE NATIONAL INSTITUTES OF HEALTH. APPLICANTS WHO USE EXPRESS MAIL OR A COURIER SERVICE ARE ADVISED TO FOLLOW THE CARRIER'S REQUIREMENTS FOR SHOWING A STREET ADDRESS. THE ADDRESS FOR THE WESTWOOD BUILDING IS:

5333 Westbard Avenue  
Bethesda, Maryland 20816